

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

Claim 1 (Withdrawn): A purified polypeptide comprising at portion of the C-terminal domain of TIMP-3; wherein said polypeptide inhibits the binding of VEGF to VEGFR2 (KDR/Flik1).

Claim 2 (Withdrawn): The polypeptide of claim 1 substantially inhibiting the binding of VEGF to VEGFR2 without substantially inhibiting the binding of VEGF to VEGFR1(Flt1).

Claim 3 (Withdrawn): The polypeptide of claim 1 being substantially free of the N-terminal domain of TIMP3.

Claim 4 (Withdrawn): The polypeptide of claim 1 being substantially free of metalloproteinase inhibiting activity.

Claim 5 (Withdrawn): The polypeptide of claim 1, the at least portion of the C-terminal domain of TIMP3 being operatively linked to a therapeutic agent.

Claim 6 (Withdrawn): The polypeptide of claim 5, the therapeutic agent being at least one of a chemotherapeutic agent, a radiotherapeutic agent, cytotoxic agent, anti-angiogenic agent, coagulant, or anti-tubulin drug.

Claim 7 (Withdrawn): The polypeptide of claim 1, the at least portion of the C-terminal domain of TIMP3 comprising SEQ ID NO:2 or variants thereof.

Claim 8 (Withdrawn): The polypeptide of claim 7, the at least portion of the C-terminal domain of TIMP3 comprising SEQ ID NO:2 or variants thereof being operatively linked to a therapeutic agent.

Claim 9 (Withdrawn): The polypeptide of claim 8, the at least portion of the C-terminal domain of TIMP3 and the therapeutic agent forming a fusion protein.

Claim 10 (Withdrawn): The polypeptide of claim 1 being capable of inhibiting the proliferation of vascular endothelial cells mediated by VEGF.

Claim 11 (Withdrawn): The polypeptide of claim 3, wherein said polypeptide is capable of inhibiting angiogenesis mediated by VEGF.

Claim 12 (Withdrawn): A pharmaceutical composition comprising the polypeptide of claim 3 and a pharmaceutically acceptable carrier.

Claim 13 (Withdrawn): A therapeutic kit comprising the pharmaceutical composition of claim 12.

Claim 14 (Currently amended): A method of inhibiting VEGF binding to the VEGF receptor VEGFR2, the method comprising contacting a cell population including cells that express VEGFR1 (FLT-1) and cells that express VEGFR2 with a composition comprising a biologically effective amount of at least one of TIMP3 or a VEGF inhibiting variant of TIMP3 fragment of TIMP3, the fragment of TIMP3 comprising SEQ ID NO: 9

Claim 15 (Currently amended): The method of claim 14, the composition not substantially inhibiting VEGF binding to VEGFR1.

Claim 16 (Currently amended): The method of claim 14, the composition comprising a ~~VEGF inhibiting~~ ~~TIMP3~~ variant the fragment of TIMP3, the fragment being substantially free of SEQ ID NO: 3 the N-terminal domain of TIMP3.

Claim 17 (Currently amended): The method of claim 14, the composition comprising a ~~VEGF inhibiting~~ ~~TIMP3~~ variant the fragment of TIMP3, the fragment being substantially free of metalloproteinase inhibiting activity.

Claim 18 (Canceled)

Claim 19 (Currently amended): The method of claim 14, the VEGF inhibiting ~~TIMP3~~ variant fragment being operatively linked to a therapeutic agent.

Claim 20 (Canceled)

Claim 21 (Original): The method of claim 19, the therapeutic agent comprising at least one of a chemotherapeutic agent, a radiotherapeutic agent, cytotoxic agent, anti-angiogenic agent, coagulant, or anti-tubulin drug.

Claim 22 (Withdrawn): A method of targeting or delivering at least one diagnostic agent or therapeutic agent to cells expressing VEGFR2 (KDR/Flik1), the method comprising operatively linking the at least one diagnostic agent or therapeutic agent to a polypeptide comprising at least a portion of the C-terminal domain of TIMP3, the at least portion of the C-terminal domain of TIMP3 being capable of readily binding to VEGFR2.

Claim 23 (Withdrawn): The method of claim 22, wherein the C-terminal domain of TIMP3 comprises at least a portion of SEQ ID NO: 2.

Claim 24 (Withdrawn): The method of claim 22, the therapeutic agent comprising at least one of chemotherapeutic agent, a radiotherapeutic agent, cytotoxic agent, anti-angiogenic agent, coagulent, or anti-tubulin drug.

Claim 25 (Withdrawn): A method of inhibiting VEGF induced endothelial cell proliferation and/or migration in a population of cells that includes VEGF and endothelial cells, the population of cells including a first concentration of TIMP3 or VEGF inhibiting TIMP3 variants, the method comprising:

increasing the concentration of at least one of TIMP3 or VEGF inhibiting TIMP3 variants in the population of endothelial cells from a first concentration to a second concentration.

Claim 26 (Withdrawn): The method of claim 25, the increase in concentration of the at least one of TIMP3 or VEGF inhibiting TIMP3 variants comprising affecting at least some cell of the population of cells to express at least one of TIMP3 or VEGF inhibiting TIMP3 variants.

Claim 27 (Withdrawn): The method of claim 25, the at least some cells of the population of cells being affected to express at least one of TIMP3 or VEGF inhibiting TIMP3 variants using gene therapy.

Claim 28 (Withdrawn): The method of claim 26, the at least some cells of the population of cells be affected to express at least one of TIMP3 or VEGF inhibiting TIMP3 variants by transfecting at least some of the cells with a vector, the vector including a nucleotide sequence encoding TIMP3 or a VEGF inhibiting variant of TIMP3.

Claim 29 (Withdrawn): A vector comprising nucleotide sequence encoding TIMP3 or a VEGF inhibiting variant of TIMP3.

Claim 30 (Withdrawn): A method of treating angiogenic disease, the method comprising:

contacting a tissue or a population of angiogenic vessels that contain vascular endothelial cells with a composition comprising a biologically effective amount of at least one of TIMP3 or VEGF inhibiting TIMP3 variants under conditions effective to inhibit VEGF induced angiogenesis and to treat angiogenic disease.

Claim 31 (Withdrawn): A method of delivering at least one of a therapeutic or diagnostic agent to angiogenic blood vessels associated with disease, the method comprising:

contacting a tissue or a population of angiogenic vessels that contain vascular endothelial cells with a composition comprising at least one of TIMP3 or VEGF inhibiting TIMP3 variants operatively linked to at least one of a diagnostic or therapeutic agent.